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## Losartan Potassium: Evaluating the Treated Aviator for Medical Waiver

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### **Literature Review**

A review of the literature concerning losartan has shown it to be a potential candidate for use in aircrew. Based on clinical studies and post-marketing surveillance, no side effects have been uncovered that would preclude aviator use *a priori*. However, a number of questions remain to be addressed before deciding whether losartan is suitable for use in military aviation. For example, data is either lacking or scant concerning cognitive, vestibular, and acceleration effects, to name a few.

### **Acceptable Candidates for Losartan**

Candidates suitable for losartan therapy are those aviators with sustained hypertension who have not responded to nonpharmacologic methods of blood pressure control. Compared to ACE inhibitors, the mode of action of losartan involves a different step along the same renin-angiotensin pathway; since there is more experience with ACE inhibitors in aircrew, the use of losartan should primarily be reserved for those who are unable to tolerate the older medications, such as drug-induced cough. It should be noted that, since angioedema has also been associated with losartan, including in one case after a previous episode of enalapril-induced angioedema, losartan is not recommended if there is a history of angioedema following treatment with ACE inhibitors.

Aviators considered for waiver of losartan therapy must show successful control of hypertension on the drug, in the standard dosage range of 50 to 100 milligrams per day, without unacceptable side effects.

### **Evaluation Process**

Since the pharmacokinetic half lives of losartan and its active metabolite, EXP-3174, are 2.1 hours and 6.3 hours, respectively, the standard washout time (5 half lives) for the metabolite would be 31.5 hours. However, because the latter is a noncompetitive antagonist at the AT<sub>1</sub> receptor, 63 to 74% of

the hypertensive effect is maintained by 4 half lives. Furthermore, there is some data suggesting a diastolic antihypertensive effect lingering for as long as a week after therapy.

Seven days prior to the initial evaluation, the aviator should discontinue therapy with losartan to allow washout prior to baseline tests. Frequent blood pressure checks should be performed over that week to rule out significant rebound hypertension off medication, although this has not been recognized with losartan. (While some degree of hypertension will undoubtedly recrudesce during this period, a few days off drug should have no significant impact, except perhaps in cases of severe hypertension. Since consistent availability of medications cannot be ensured under wartime conditions, disease of that severity should raise questions as to the member's fitness for continued military aviation.) After the washout period, baseline testing will be performed. The drug will then be restarted at the prior dosage. After 72 hours on the drug, those tests which need to be repeated will be performed. In addition, high performance aviators will undergo acceleration testing according to the proficiency profile of their air frame.

### **Tests to be Performed**

These are outlined under the "Gold Standards" chapter. Acceleration testing would only be performed in high performance aviators. If results of testing showed no unacceptable drug effects, return to flying status would be favorably considered.

### **Follow-up**

The aviator should be reevaluated in 6-12 months. Organ systems which may typically develop delayed drug side effects, such as the eye, will be reevaluated at that time. If the results of such testing are acceptable, subsequent follow-up will be according to usual policy.

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